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- as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)
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- with international search report

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: A NOVEL PROCESS FOR AMORPHOUS FORM OF DONEPEZIL HYDROCHLORIDE

(57) Abstract: The present invention provides a novel process for the preparation of donepezil hydrochloride.

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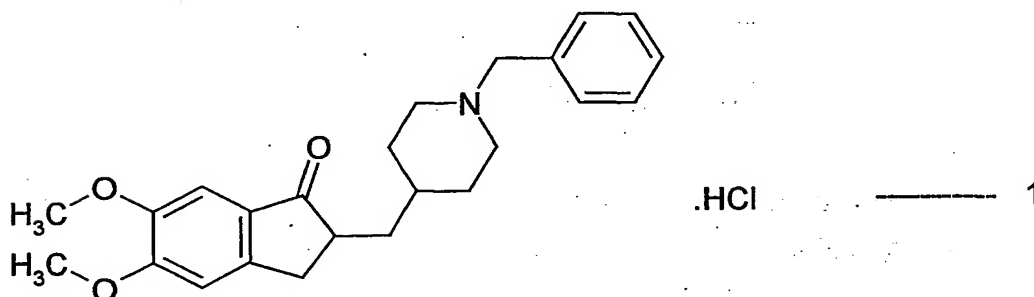
A NOVEL PROCESS FOR AMORPHOUS FORM OF DONEPEZIL
HYDROCHLORIDE

FIELD OF THE INVENTION

5 The present invention provides a novel process for the preparation of donepezil hydrochloride.

BACKGROUND OF THE INVENTION

10 Donepezil hydrochloride of formula (1):



15 or 2,3-Dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1H-inden-1-one hydrochloride is useful for prevention and treatment of alzheimer disease. The therapeutic uses of donepezil hydrochloride and related compounds are disclosed in EP 296560. Amorphous form of donepezil hydrochloride is mentioned in US 6,140,321.

20 We have discovered a simple novel process for the preparation of amorphous form of donepezil hydrochloride.

 The object of the present invention is to provide a novel process for the preparation of the amorphous of donepezil hydrochloride.

DETAILED DESCRIPTION OF THE INVENTION

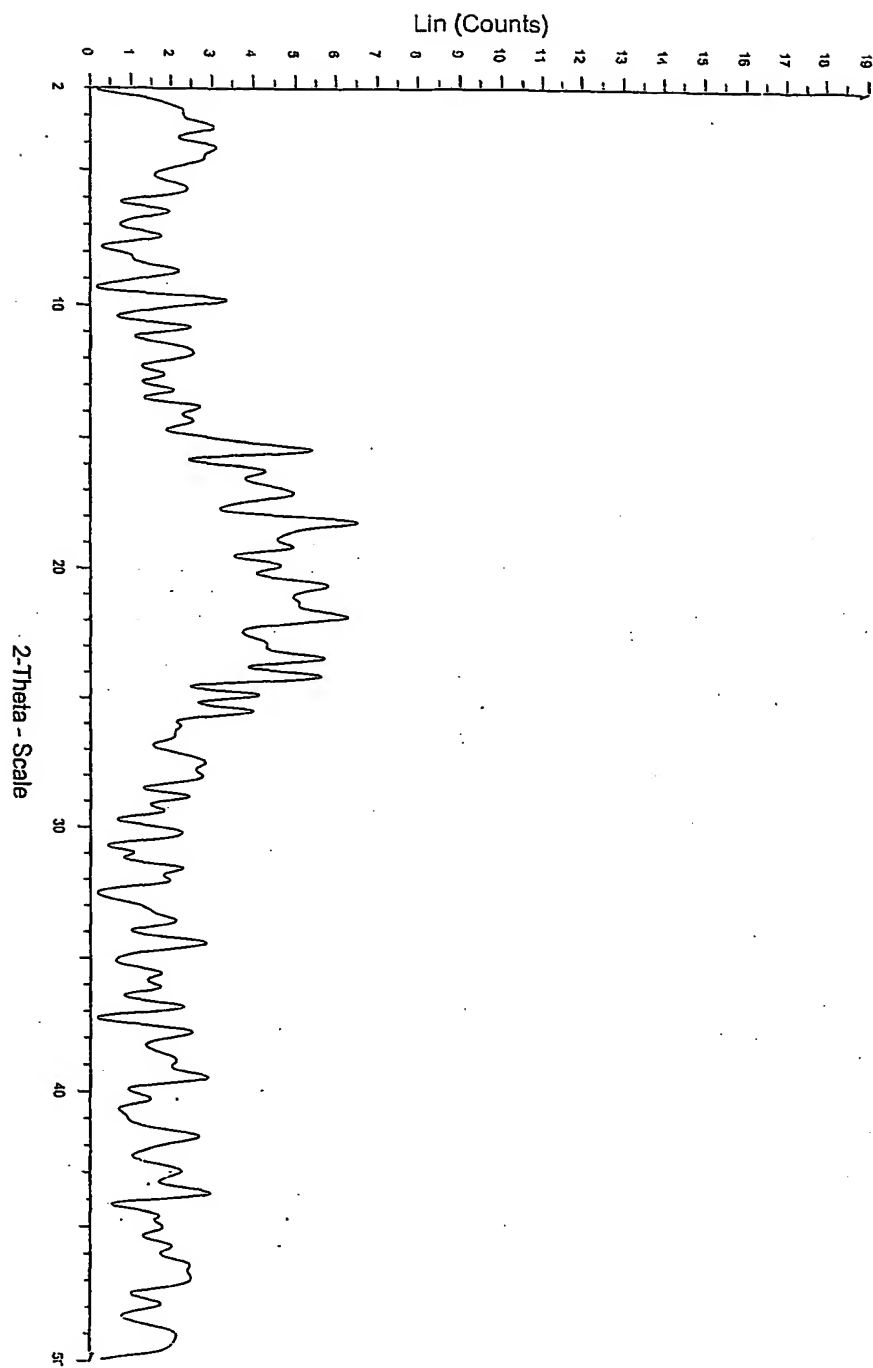
25 The amorphous donepezil hydrochloride is characterized by having broad x-ray diffraction spectrum as in figure 1.

Crystalline donepezil hydrochloride (10 gm) is dissolved in the mixture of ethanol (60 ml) and chloroform (50 ml). The solution is subjected to vacuum drying at about 45°C for 9 hours to give 9.2 gm of amorphous donepezil hydrochloride.

5

Example 4

Example 3 is repeated by subjecting the solution to spray drying using nitrogen gas instead of vacuum drying to give amorphous donepezil hydrochloride.



INTERNATIONAL SEARCH REPORT

International application No.
PCT/IN 03/00136-0

CLASSIFICATION OF SUBJECT MATTER

IPC⁷: C07D 211/32

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC⁷: C07D 211/32

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPOQUE: WPI, PAJ, EPODOC, NPL, MEDLINE, XPESP databases; STN Karlsruhe CAS: REGISTRY and CA databases

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5985864 A (IMAI ET AL.) 16 November 1999 (16.11.99) <i>example 108.</i>	1-4
A	EP 1048653 A1 (ESAI CO., LTD.) 2 November 2000 (02.11.00) <i>examples.</i>	1-4

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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„T“ later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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„Y“ document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

„&“ document member of the same patent family

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Information on patent family members

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PCT/IN 03/00136-0

Patent document cited in search report			Publication date	Patent family member(s)			Publication date
EP	A	1048653	2000-11-02	US	B	6245911	2001-06-12
				WO	A	9929668	1999-06-17
US	A	5985864		CA	A	2252806	1997-12-11
				DE	T	69718216T	2003-10-09
				TW	B	513409	2002-12-11
				ES	T	2188946T	2003-07-01
				PT	T	1019374T	2003-03-31
				DK	T	1019374T	2003-04-07